

Geminivirus Rep Protein Interferes with the Plant DNA Methylation Machinery and Modifies the Host Epigenome

Edgar Rodríguez-Negrete, Alvaro Piedra-Aguilera, Lucia Cruzado, Eduardo R. Bejarano and Araceli G. Castillo

Area de Genética. Instituto de Hortofruticultura Subtropical y Mediterránea “La Mayora”, Universidad de Málaga-Consejo Superior de Investigaciones Científicas (IHSM-UMA-CSIC). Campus Teatinos. 29071-Málaga, Spain.

The apparent simplicity of viruses hides the complexity of their interactions with their hosts. Viruses are masters at circumventing host defenses and manipulating the cellular environment for their own benefit. The replication of the largest known *family* of single-stranded DNA viruses, *Geminiviridae*, is impaired by DNA methylation and *Arabidopsis* mutants affected in cytosine methylation are hypersusceptible to geminivirus infection. This implies that plants might use methylation as a defense against geminiviruses and that the viral genome is a target for plant DNA methyltransferases. We have found a novel counter-defense strategy used by geminiviruses, that reduces the expression of the plant maintenance DNA methyltransferases, *MET1* and *CMT3*, in both, locally and systemically infected tissues. Furthermore, we demonstrated that the virus-mediated repression of these two maintenance DNA methyltransferases is widely spread among different geminivirus species. Additionally, we identified Rep as the geminiviral protein responsible for the repression of *MET1* and *CMT3*, and another viral protein, C4, as an ancillary player in *MET1* downregulation. The presence of Rep, suppresses TGS of an *Arabidopsis* transgene and of host loci whose expression is strongly controlled by CG methylation. Bisulfite sequencing analyses showed that the expression of Rep caused a substantial reduction in the levels of DNA methylation at CG sites. Our findings suggest that Rep, the only viral protein essential for geminiviral replication, displays TGS suppressor activity through a mechanism distinct from the one thus far described for geminiviruses.